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13. Abstract ***(Maximum 200 Words)*** *(abstract should contain no proprietary or confidential information)*
Achieving tumor-free margins is an important clinical goal in breast conservation surgery for the treatment of breast cancer. This prospective observational study was designed to answer: can radiography be used to exclude negative margins in breast cancer specimens? Ninety-seven cancers in 95 patients were included in this study. Pathology was used as the gold standard in specimen analysis, each containing 6 (superior, inferior, lateral, medial, anterior, posterior) margins. Of the 582 specimens, there were 8 true positive, 463 true negative, 91 false negative, and 20 false positive margins. The following performance parameters were calculated: sensitivity 8%, specificity 96%, accuracy 81%. Overall, specimen radiography cannot be reliably used to diagnose positive margins, nor can it be used to exclude negative margins.

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INTRODUCTION

Breast cancer is a major cause of morbidity and mortality in the United States (1). In women, it is the most common cancer and second leading cause of cancer deaths. With widespread implementation of screening mammography, breast cancer is now diagnosed at an earlier stage, often prior to the onset of clinical symptoms when the cancer is non-palpable (2). As many of these early-stage cancers can be visualized only through mammography, tissue specimens are routinely radiographed to ensure proper excision (3-5). Compression of the excised tissue is considered a necessary technical component for optimal imaging. Image-guided core biopsy allows many breast cancers to be diagnosed prior to surgical excision (6,7). This pre-operative diagnostic information allows the surgeon to perform the definitive excisional procedure at first surgery. Nevertheless, as many as 50% of breast cancer patients who choose breast conservation surgery need to undergo subsequent re-excision surgeries prior to obtaining cancer-free margins.

BODY

Materials and Methods

This is a prospective observational study (approved by Institutional Review Board) based at Brigham and Women's Hospital, Harvard Medical School (Boston, MA), consisting of radiologic and pathologic analyses of breast cancer specimens during a 12-month period. Demographic data were gathered from clinical notes. Each specimen was aligned on a grid for internal control, with 4 edges representing the superior, inferior, lateral, and medial margins. This aligned specimen was imaged 3 times: 1) with no compression; 2) at half-compression (defined as 9 decaNewton); 3) at full compression (defined as 18 decaNewton). It was then re-aligned with the 4 edges representing the anterior, posterior, lateral, and medial margins (i.e. orthogonal projection) and re-imaged for the fourth time (at full compression). Information on margin orientation was obtained from the inking or suturing on the specimen, provided by the operating surgeon. Hence, any breast cancer specimens without this margin orientation information (e.g. "uninked specimen") was excluded from the study. Cancers that were visualized only by ultrasound or magnetic resonance imaging were also excluded from the study, as were cancers that were sufficiently removed by core biopsy so that there were no longer any mammographic targets.

Each square on the grid (upon which the specimen is radiographed) measured 2 cm. This grid served as internal control for measurements. The location of the cancer within the specimen with respect to each of the 6 margins was analyzed, using the 2 specimen radiographs obtained at full compression (but in orthogonal projections). Full compression was selected for analysis in this study, as this is the compression state of the

specimen when it is received by the interpreting pathologist. At radiologic analysis, "positive margin" was defined as the presence of cancer within 5 mm of the specimen edge. At pathologic analysis, "positive margin" was defined as the presence of cancer less than 1 mm of the inked edge. Pathologic analysis was used as the "gold standard" in this study, while radiologic analysis was the test. Hence, true positive (TP) and true negative (TN) were defined as agreement at radiologic and pathologic analyses as to the presence and absence of cancer at the margin, respectively. False positive (FP) was defined as the presence of cancer at the margin at radiologic analysis, but absence of cancer at the margin at pathologic analysis. False negative (FN) was defined as the absence of cancer at the margin at radiologic analysis, but presence of cancer at the margin at pathologic analysis.

The 3 specimen radiographs obtained at 3 different levels of compression (but in same projection) were compared with the initial mammogram. They were rated 1) worse; 2) same; or 3) better than the initial mammogram in depicting the cancer.

Results

This study consists of 97 breast cancer specimen radiographs in 95 women, performed between October 2001 and September 2002. (Two patients had two distinct sites of cancer each.) All the patients in this study were female. The patients ranged in age from 34 to 92 years (median age 57 years). The following demographic data (family history of breast cancer, personal history of breast cancer, menopausal status, hormone replacement therapy) were collected and presented in **Table 1**.

Both invasive cancers and ductal carcinoma in-situ (DCIS) cases were included in this study. There were 66 (68%) invasive cancers, 29 (30%) cases of DCIS only, and 2 phyllodes tumors (2%). The histologic types of the cancers are presented in **Table 2**. Of the 97 cancers in this study, 40 (41%) presented as calcifications, and 57 (59%) as masses. Size of lesions ranged from 1 to 60 mm (median size 10 mm) for calcifications and from 5 to 12 mm (median size 45 mm) for masses. Overall, cancers in this study ranged in size from 1 to 60 mm (median size 10 mm). Eighty-three cancers (86%) were detected at mammographic screening, while 7 (7%) presented with clinical symptoms of either a palpable lump (n=6) or focal pain (n=1). No information on mode of presentation was ascertained in 7 (7%) cases.

Eighty-five (88%) of the 97 cancers in this study were initially diagnosed by core biopsy, and 12 (12%) underwent surgical excision without pre-operative core biopsy diagnosis. Reasons why cancers were not first sampled by core biopsy are summarized in **Table 3**. Fifty-one (60%) of the 85 cancers that were first diagnosed by core biopsy were sampled at our institution, while 34 (40%) were sampled at an outside referring institution. Of 97 cancers in this study, 37 (38%) were recommended by a staff

radiologist within our institution, and 60 (62%) were referred from an outside institution for surgical excision.

Table 4 compares the positive and negative findings at specimen radiography with those at pathologic analysis. Each specimen constitutes 1 case, and each specimen has 6 margins. The numbers provided in Table 4 are provided in units of margins (not cases). Using pathology as the "gold standard" in determining the presence or absence of cancer at the specimen margin, a 4 x 4 table was created (**Table 4**) in calculating the performance characteristics of specimen radiography. The following results were calculated: sensitivity 8%; specificity 96%; positive predictive value (PPV) 29%; negative predictive value (NPV) 84%; accuracy 81%.

The sensitivity of specimen radiography is low in this study. In 58 cases, specimen radiography was insufficient in predicting the presence of cancer at one or more margins(s) (**Figure 1 a-b**). These observations concur with the accepted practice that radiography cannot be used to exclude microscopic disease (8-10). But can specimen radiography be used to exclude negative margins? There were only 8 true positive (**Figure 2 a-d, Figure 3 a-b**) margins in this study of 582 margins. This is not surprising, as every surgeon aims to attain negative margins at excision. In other words, the pre-test probability of having positive margins is low, reflected in the low PPV of 29%.

More importantly, there were 13 false positive (**Figure 1 a-b**) cases in this study. False positive cases may result in unnecessary excision of more tissue, which in turn may result in increased scarring and operating/anesthesia time. Review of the data showed that in the 13 cases where there was at least 1 false positive margin, only 2 cases would

have resulted in unnecessary further excision. In the remaining 11 cases, 1 or more of the 6 margins was either true positive or false negative, which would have required further excision.

How much clinical impact do positive margins have on patient management? Of the 95 patients in this study, 36 (38%) underwent at least 1 re-excision surgery. One additional patient was scheduled to undergo re-excision surgery at the time of this report, and a second patient was unable to undergo re-excision surgery because of severe chronic obstructive pulmonary disease.

Does pre-operative core biopsy impact the need for re-excision surgery? **Table 5** shows that number of patients who underwent at least 1 re-excision surgery as a function of the presence or absence of pre-operative core biopsy. If a patient is first diagnosed as having cancer through pre-operative core biopsy sampling, then the probability that she will need re-excision surgery is 36%. If a patient does not have a pre-operative diagnosis of cancer, then the probability that she will need re-excision surgery increases to 73%. In other words, the relative odds of needing re-excision surgery for a patient without pre-operative core biopsy (compared with the patient with pre-operative core biopsy) is 2.1. The relative odds of not needing re-excision surgery for a patient with pre-operative core biopsy (compared with the patient without pre-operative core biopsy) is 2.4.

The quality of specimen radiography at the 3 compression levels in depicting cancer was assessed (Figure 2 a-c). The results are presented in **Table 6**. In the majority of cases, radiographs obtained with no compression are worse than the initial mammogram (73/97 or 75%), and radiographs obtained at half- or full-compression are better than the initial mammogram (58/97 or 60%, and 76/97 or 78%, respectively).

Limitations

Case recruitment

1. Many patients underwent pre-operative core biopsy with large-gauge needles that occasionally resulted in complete removal of the initial mammographic target. In such cases, a stainless steel clip was used to mark the site of cancer for clinical management, but such cases were not appropriate for this study. This occurred particularly frequently in cases of DCIS that manifested as clustered microcalcifications.
2. Patient recruitment was further limited by the sizable number of cancers that were seen only on ultrasound. While specimen ultrasound can be employed, this technique is limited by operator dependence and was not included in the study design.
3. Some patients did not or were not able to provide accurate and complete demographic data.
4. In the majority of cases, the radiographically visible cancer wa not located close to the specimen edge, as the clinical goal was complete excision of the lesion with clear margins. Hence, the number of true positive margins was low in the study. In other words, the pre-test probability that any one piece of specimen would have positive margin(s) was low. This necessitated a large sample size.

Radiographing specimen

1. Because of varying size and shape of specimens, proper placement of photocell for optimal radiography was difficult and variable on a case-by-case basis.
2. In a few cases, very large pieces of excised tissues could not fit on one single image for analysis.

Specimen radiograph interpretation and margin assessment

1. At times, it was difficult to determine the constituents of cancer on specimen radiograph. In-vivo radiography within the patient's breast (initial mammography) differed technically from ex-vivo radiography within the excised tissue (specimen radiography). In specimen radiography, spiculations were more prominent, and calcifications previously not visible during in-vivo imaging may became visible. Prior to determining the utility of specimen radiography in excluding negative margin(s), one needed to establish which imaging features constituted cancer. For example: a) Were spiculations part of the cancer, or were they merely the body's desmoplastic response to the cancer (**Figure 2 c-d**)? Was the answer case-dependent? b) Which calcifications represented cancer necrosis, and which represented fibrocystic change (**Figure 4**)?
2. Surgical ink, metallic wires, and metallic clips occasionally obscured visualization of the mammographic target, limiting margin assessment.
3. Most specimens were irregular in three-dimensional shape and not a true cube. Hence, determination of where one margin ended and another margin began was approximate.

Compression assessment

1. Compression was technically limited in cases of hard, palpable cancers (which tended to resist compressive force). This occurred most frequently when compressing in the orthogonal projection (**Figure 2d**).

TABLE 1. Demographic information in 95 patients

Family history of breast cancer	
Yes	30 (32%)
No	40 (42%)
Unknown	25 (26%)*
Personal history of breast cancer	
Yes (ipsilateral breast)	2 (2%)
Yes (contralateral breast)	8 (8%)
No	67 (71%)
Unknown	18 (19%)
Menopausal status	
Pre-menopausal	30 (32%)
Post-menopausal	60 (63%)
Unknown	5 (5%)
Exogenous hormone therapy	
Yes	14 (15%)**
No	59 (62%)
Unknown	22 (23%)

* including 2 patients who were adopted

** including 13 patients receiving hormone replacement therapy and 1 patient receiving oral contraceptive pill

TABLE 2. Histologic types of 97 cancers: invasive, in-situ, and phyllodes

Invasive cancer	
Invasive ductal carcinoma, not otherwise specified	44 (45%)
Invasive carcinoma, mixed ductal and lobular	9 (10%)
Invasive lobular carcinoma	8 (9%)
Invasive mucinous carcinoma	3 (3%)
Ductal carcinoma in-situ	29 (30%)
Phyllodes	2 (3%)

Percentages were rounded up for sum of 100%.

TABLE 3. Reasons why 12 cancers did not undergo pre-operative core biopsy

Mammographic lesion was too faint or too subtle	5 (42%)
Known cancer at same site from prior excision	2 (17%)
Surgery planned for ipsilateral cancer (at different site)	2 (17%)
Cannot lie prone on stereotactic core biopsy table	1 (8%)
Cardiac condition	1 (8%)
Unknown	1 (8%)

Table 4. Performance characteristics of specimen radiography in predicting the presence of cancer at specimen margins. Analysis was performed of 97 cancers, each with 6 margins. (Total number of margins = 582)

	Pathologic analysis (disease)	
	Positive margins	Negative margins
Specimen radiography (test)		
Positive margins	8	20
Negative margins	91	463

Sensitivity: TP/TP+FN 8/8+91 = 0.08 = 8.1%

Specificity: TN/TN+FP = 463/463+20 = 95.9%

Positive predictive value: TP/TP+FP = 8/8+20 = 28.6%

Negative predictive value: TN/TN+FN = 463/463+91 = 83.6%

Accuracy: TP+TN/TP+TN+FP+FN = 8+463/8+463+20+91 = 80.9%

Table 5. Occurrence of re-excision surgery (due to positive margins) in 95 patients as function of pre-operative core biopsy

	Re-excision surgery	
	Yes	No
Pre-operative core biopsy		
Yes	30	54
No	8	3

Table 6. Quality of specimen radiograph when compared with initial mammogram in 97 cancers

	Compression		
	No	Half	Full
Worse than initial mammogram	74	0	3
Same as initial mammogram	16	39	17
Better than initial mammogram	7	58	77

KEY RESEARCH ACCOMPLISHMENTS

- Tumor detection at margins of specimen radiography is not indicative of positive specimen margins at pathologic analysis. Hence, radiography cannot be used to exclude negative margins.
- Absence of tumor detection at margins of specimen radiography does not exclude positive specimen margins at pathologic analysis. Hence, specimen radiography cannot be used to predict positive margins.
- Some amount of specimen compression is necessary to radiographically depict cancer at least as well as the initial mammogram.
- Even at half compression, specimen radiography depicts cancer better than initial mammography in most cases.
- Specimen radiography at full compression depicts cancer better than specimen radiography at half compression in most cases.
- The majority of breast cancers are diagnosed pre-operatively by means of core biopsy, allowing the surgeon to better perform the definitive operation at first surgery. The patient is less likely to undergo re-excision if her cancer is diagnosed pre-operatively by means of core biopsy.
- Many of our breast cancer cases are referred from community hospitals to our tertiary care institution for surgical treatment. A significant number of these referral cases are diagnosed by means of core biopsy at the community hospital, reflecting the widespread prevalence and availability of core biopsy.

REPORTABLE OUTCOMES

Through this project, I have learned about various aspects of conducting prospective clinical research (versus retrospective review), including patient recruitment, obtaining approval from Institutional Review Board (IRB), database building, data collection and analysis, and formation of observations with clinical relevance. This experience has also taught me about securing and utilizing extramural grant support, and I am preparing to apply for a K-grant from the National Institutes of Health to support my research career in breast imaging. Beginning November 1, 2002, I will embark on a research career track in which my position will be composed of 50% research work and 50% clinical work.

I have presented these research results at our institutional research meeting, and I am preparing an article based on these results to be submitted to a peer-reviewed radiology journal (either *Academic Radiology* or *Breast Journal*) for publication.

CONCLUSIONS

The majority of breast cancer patients choose breast-conservation surgery (lumpectomy) over mastectomy when medically feasible. The goal of lumpectomy is complete removal of malignancy with a margin of normal (cancer-free) tissue. Achieving cancer-free margins is an important clinical end-point, as recurrence is proportional to residual local disease (11-13). The breast surgeon strives to achieve cancer-free margins while optimizing the cosmetic outcome of breast-conservation surgery.

The utility of specimen radiography in predicting pathologic outcomes has been examined from various perspectives (8-10). This study was designed to examine specifically cases in which radiographic evidence of cancer was present at the edge(s) of excised tissue; it was not aimed to show that radiologic analysis could replace pathologic analysis. Indeed, the study demonstrated many cases of positive margins that were not visible on specimen radiograph. Though there were true positive cases in which specimen radiographic findings correlated with positive margins, there were also false positive cases in which no cancer was found at the margins despite the presence of radiologic lesion at the edge of the specimen radiograph. Hence, at this time, radiography cannot be used to exclude negative margins in breast cancer specimens. In other words, specimen radiography cannot be used reliably to guide the surgeon intra-operatively to resect more tissue prior to skin closure. This one-year study was limited by the relatively small number of cases in which positive margins were present. Future studies consisting of larger case accrual will further address this question.

This study also examined the effects of compression on the quality of specimen radiography. While compression is known to be necessary, it is also known to affect pathologic analysis of breast cancer specimens (14,15). These results suggest that half (versus full) compression is often sufficient in confirming the presence of the mammographic target within the specimen. Future studies may confirm or negate this observation and examine whether the degree of compression is proportional to the degree of tissue distortion at pathologic analysis.

REFERENCES

1. Greenlee RT, Murray T, Bolden S, Wingo PA. Cancer Statistics, 2000, Ca Cancer J Clin, 2000; 50:7-33.

2. Feig S. Decreased breast cancer mortality through mammographic screening: results of clinical trials, 1988; 167:659-665.

3. Holland R. The role of specimen x-ray in the diagnosis of breast cancer, Diagn Imag Clin Med; 1985; 54:178-185.

4. Gallager HS. Breast specimen radiography, Am J Clin Pathol 1975; 64:749-755.

5. Snyder RE. Specimen radiography and preoperative localization of nonpalpable breast cancer, Cancer 1980; 46:950-956.

6. Meyer JE, Smith DN, Lester SC, et al. Large-core needle biopsy of nonpalpable breast lesions, JAMA 1999; 281:1638-1641.

7. Margolin FR, Leung JW, Jacobs RP, Denny SR. Percutaneous imaging-guided core breast biopsy: 5 years' experience in a community hospital, AJR 2001; 177:559-564.

8. Graham RA, Homer MJ, Sigler CJ, et al. The efficacy of specimen radiography in evaluating the surgical margins of impalpable breast carcinoma, AJR 1994; 162:33-36.

9. Dixon JM, Sekar OR, Walsh J, Paterson D, Anderson TJ. Specimen-orientated radiography helps define excision margins of malignant lesions detected by breast screening, Br J Surg, 1993; 80:1001-1002.

10. Lee CH, Carter D. Detecting residual tumor after excisional biopsy of impalpable breast carcinoma: efficacy of comparing preoperative mammograms with radiographs of the biopsy specimen, 1995; AJR 164:81-86.

11. Shulman M, Sadfarangani GJ. Breast cancer-importance of adequate surgical excision prior to radiotherapy in the local control of breast cancer in patients treated conservatively, Arch Surg 1992; 127:411-415.

12. Neuschatz AC, DiPetrillo T, Safaii H, Lowther D, Landa M, Wazer DE. Margin width as a determinant of local control with and without radiation therapy for ductal carcinoma in situ of the breast, Int J Cancer 2001; 96:97-104.

13. Neuschatz AC, DiPetrillo T, Steinhoff M, et al. The value of breast lumpectomy margin assessment as a predictor of residual tumor burden in ductal carcinoma in situ of the breast, Cancer 2002; 94:1917-1924.

14. Birdwell RL, Ikeda DM, Dirbas F, Bergman G, Jeffrey SS. Does breast tissue specimen radiography require compression? [abstract], AJR 2000; 174(supp):24.

15. Graham RA, Homer MJ, Katz J, Rothschild J, Safaii H, Supran S. The pancake phenomenon contributes to the inaccuracy of margin assessment in patients with breast cancer, Am J Surg 2002; 184;89-93.

APPENDICES

FIGURE 1a. False negative (inferior margin) specimen radiograph at full-compression. A 20-cm irregular mass was visualized in the middle of the excised tissue, not involving any of the 4 margins (lateral, medial, superior, inferior) at radiologic analysis. At pathologic analysis, this mass represented an invasive ductal carcionoma, and cancer was identified at the inferior margin. Hence, this is an example of a false negative margin.

Superior

Lateral

Medial

Inferior

FIGURE 1b. False negative (posterior margin) and false positive (anterior margin) specimen radiograph at full-compression in the orthogonal projection. This is the same specimen as figure 2a, except that it has been compressed in the orthogonal projection so that the anterior and posterior margins are now imaged (versus the superior and inferior margins). The irregular mass (representing invasive ductal carcinoma) appeared to extend to the anterior margin. However, on pathologic analysis, no cancer was found at the anterior margin (false positive). Rather, cancer was found at the posterior margin (false negative).

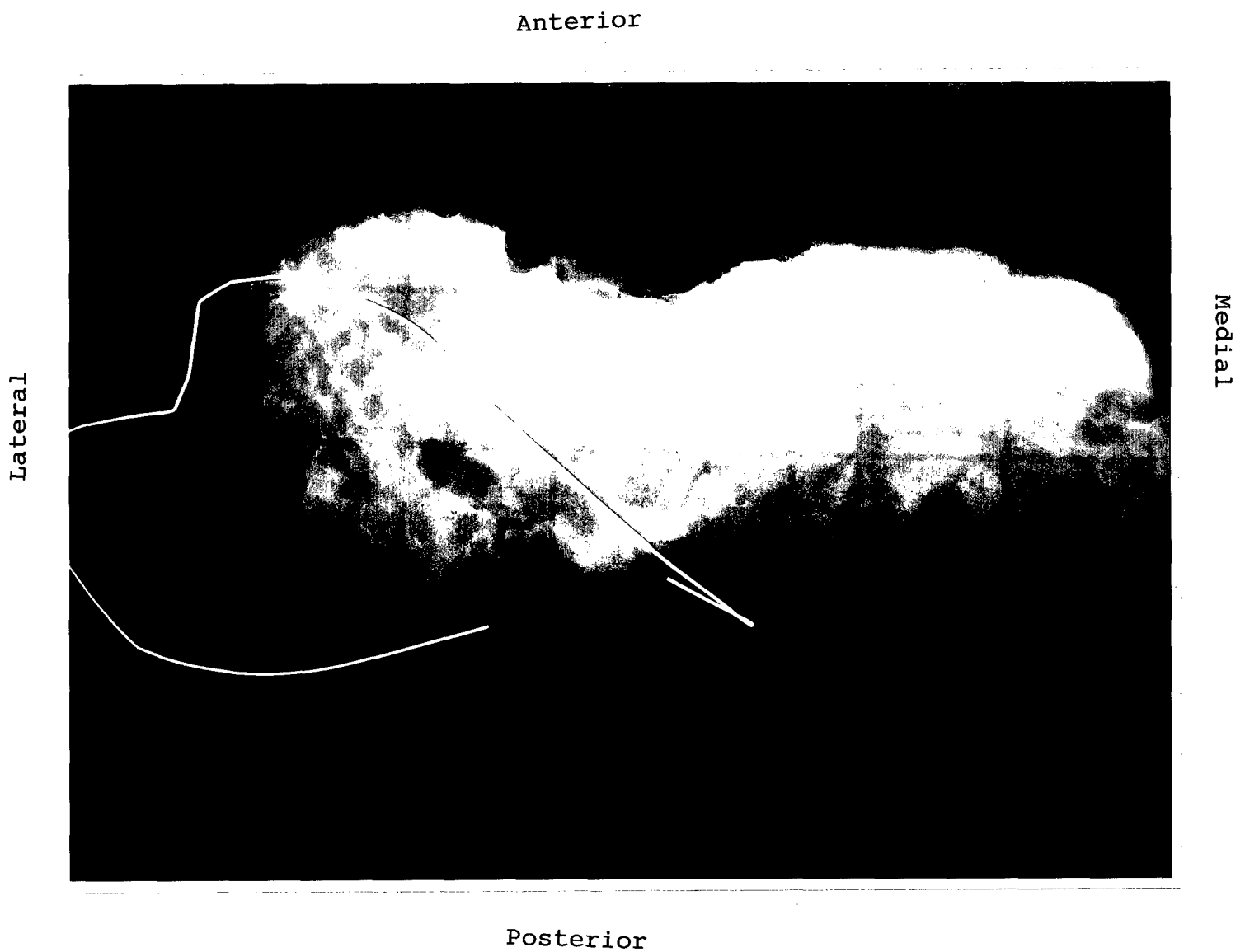


FIGURE 2a. True positive (lateral margin) specimen radiograph with no compression. Each square represented 20-mm. A 40-mm spiculated mass was localized and excised. The distal aspect of the hookwire was present, but the mass was poorly seen. Benign-appearing, round, punctate calcifications were also present. Pathologic analysis revealed an invasive ductal carcinoma, with cancer present at the lateral margin.

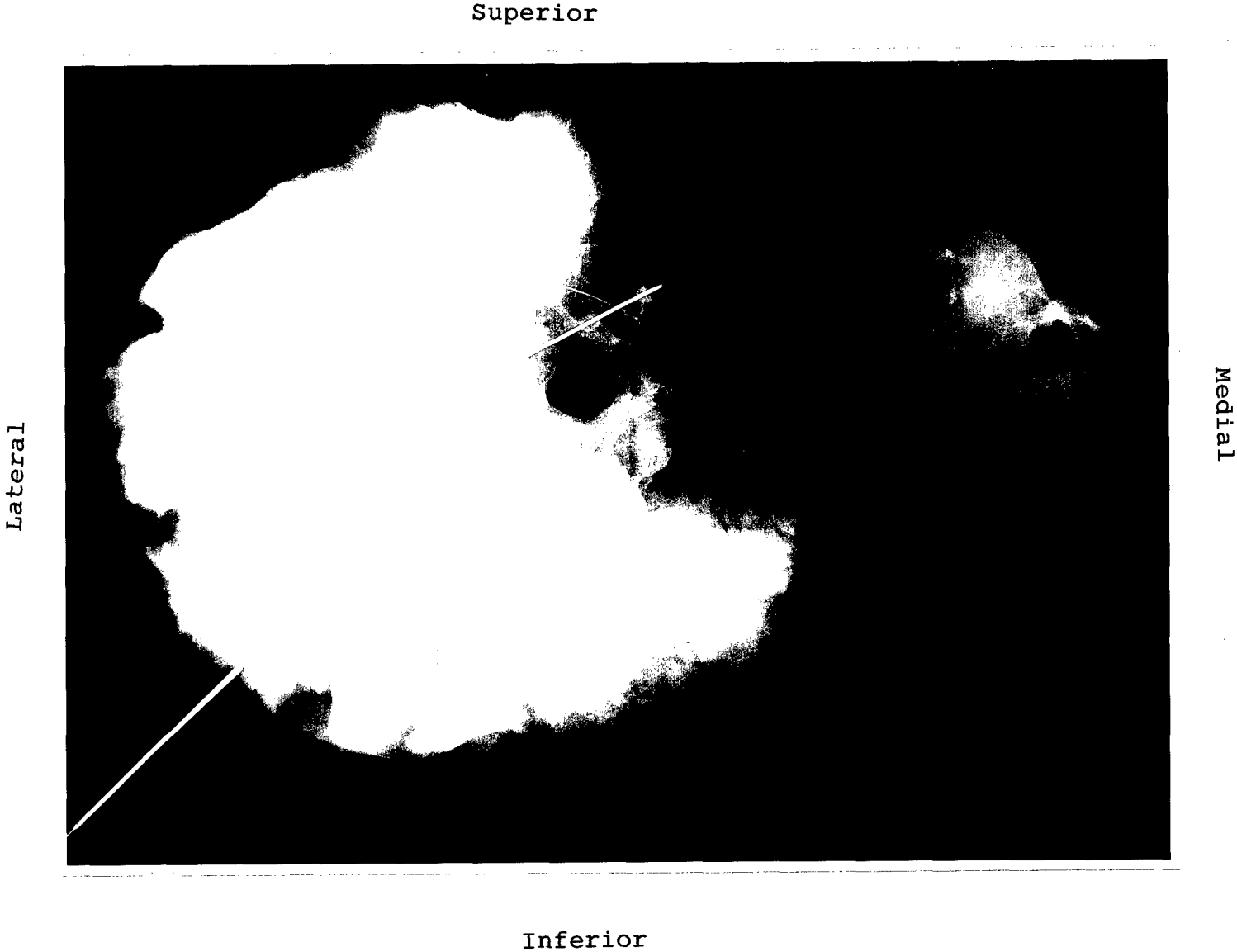


FIGURE 2b. True positive (lateral margin) specimen radiograph at half-compression. The spiculated mass, representing invasive ductal carcinoma, was better seen at half-compression than with no compression.

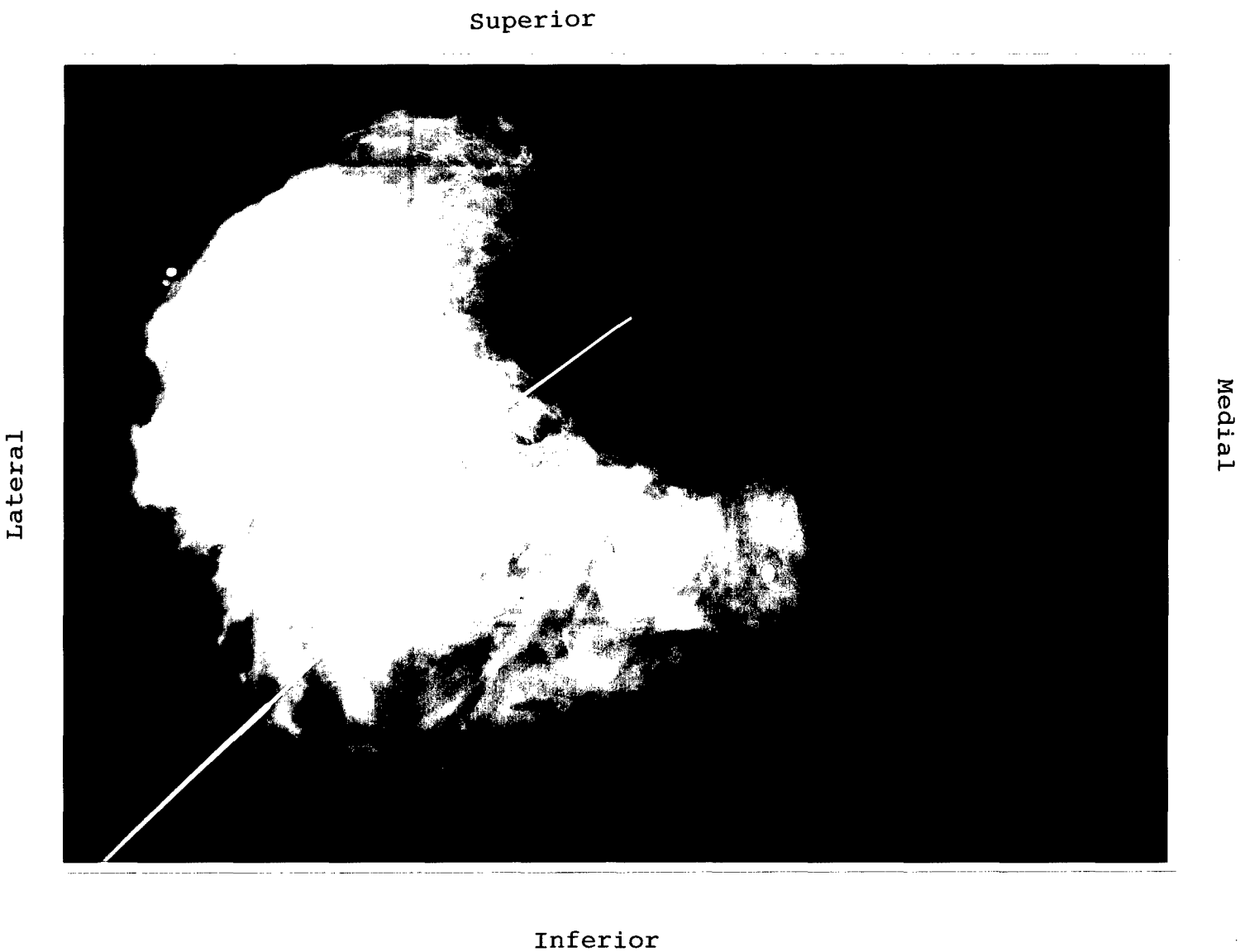


FIGURE 2c. True positive (lateral margin) specimen radiograph at full-compression. The spiculated mass, representing invasive ductal carcinoma, was well seen at full-compression, extending to the lateral edge of the excised specimen. Pathologic analysis revealed the presence of cancer at the lateral margin.

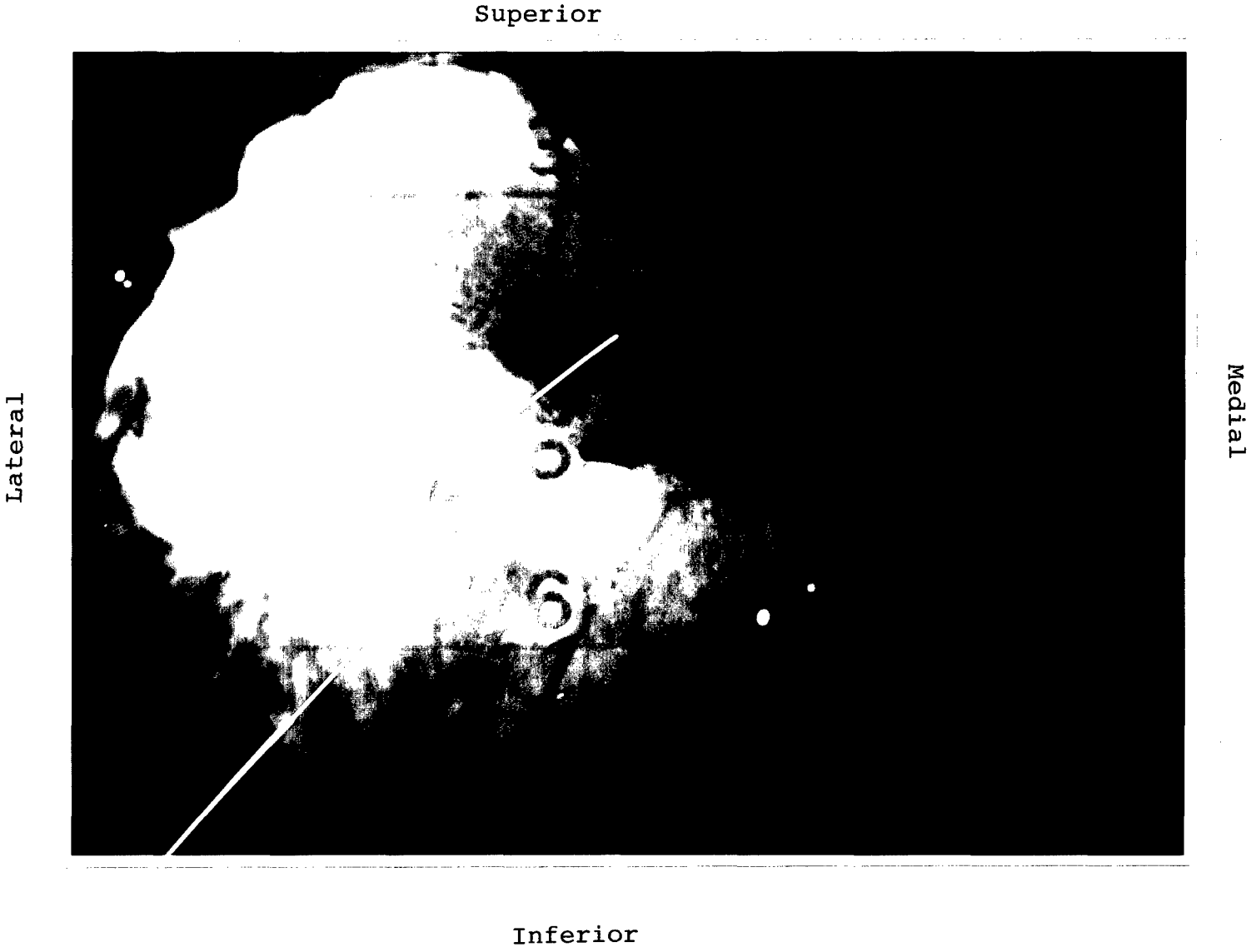


FIGURE 2d. True positive (lateral margin) specimen radiograph at full-compression in the orthogonal projection (demonstrating anterior and posterior margins versus superior and inferior margins). Note that this orthogonal projection did not vary much from the initial projection (see figure 2c), as the firm nature of the cancer mass prevented complete compression in the true orthogonal projection. Note also that the spiculated mass was again seen at the lateral edge.

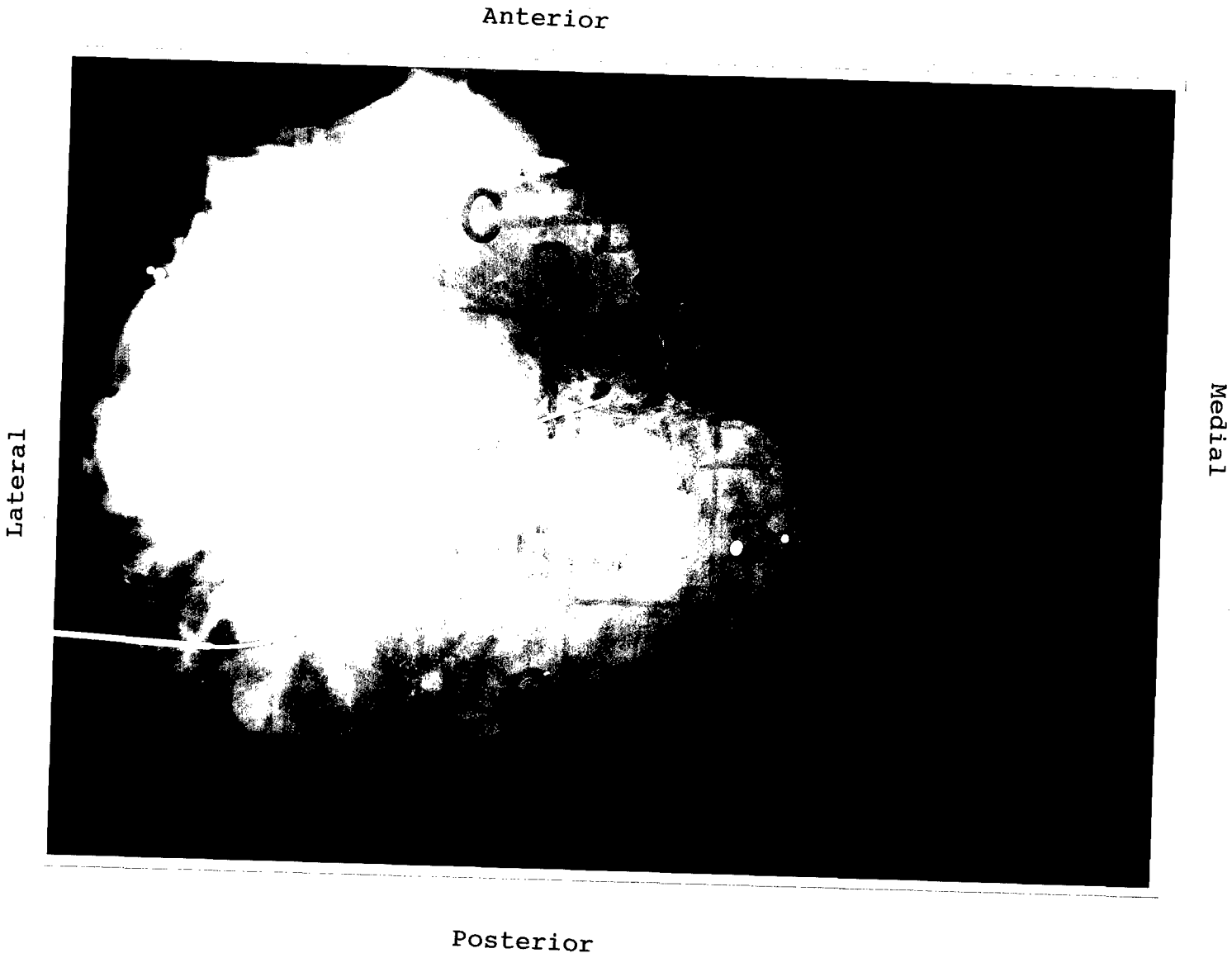
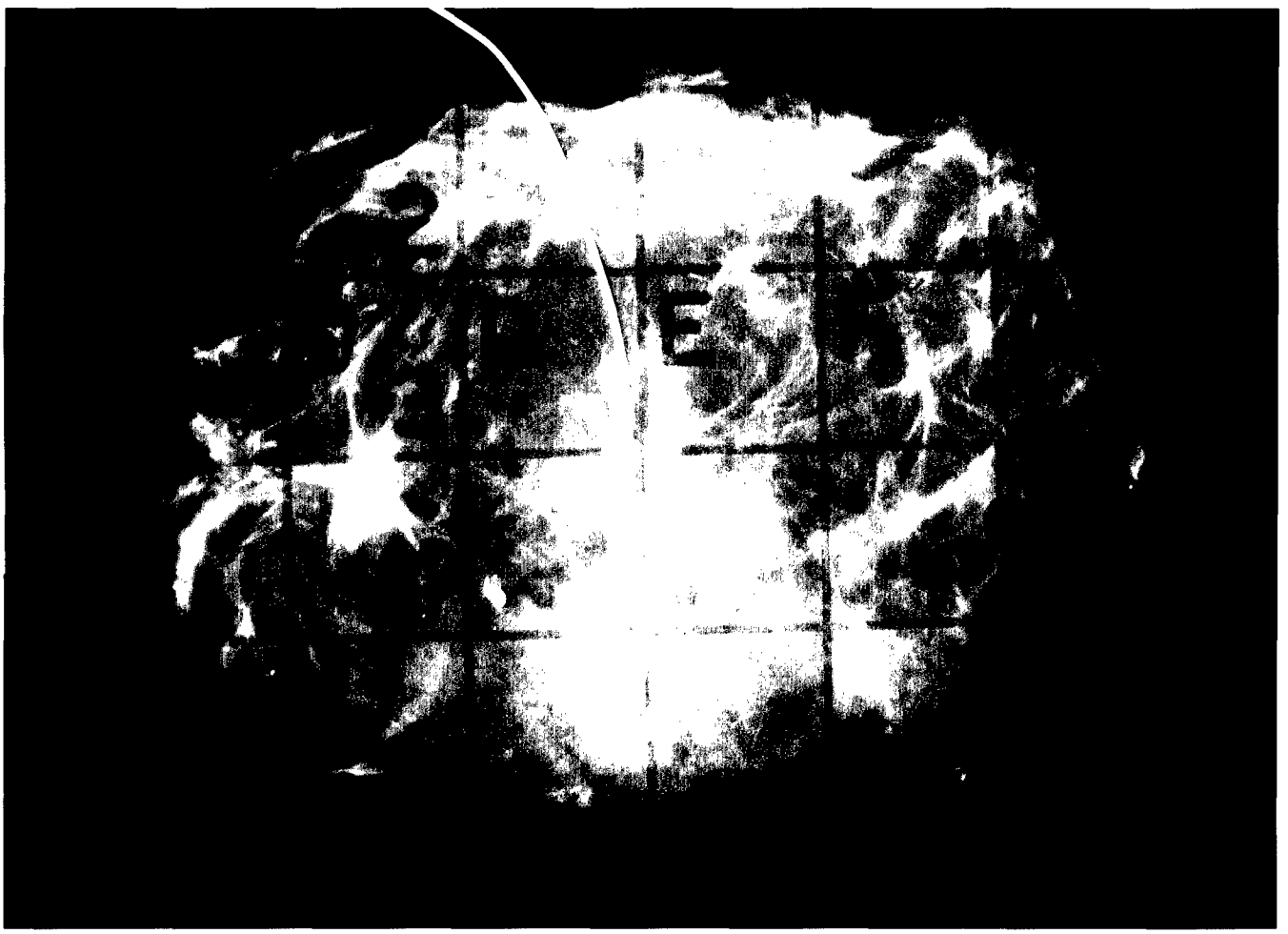


FIGURE 3a. True negative (lateral, medial, superior, inferior margins) specimen radiograph at full-compression. A 5-mm cluster of pleomorphic microcalcifications is identified, representing high-grade ductal carcinona in-situ. These calcifications are situated in the middle of the specimen (at the thick part of the wire), without involving any of the 4 margins imaged. Pathologic analysis confirmed this radiologic observation.

Superior



Lateral

Medial

Inferior

FIGURE 3b. True negative (lateral, medial, anterior, posterior margins) specimen radiograph at full-compression in the orthogonal projection. This is the same specimen as figure 3c. The anterior and posterior margins are imaged (versus the superior and inferior margins). The microcalcifications remain situated in the middle of the specimen (at the thick part of the wire), without involving any of the 4 margins imaged. Pathologic analysis confirmed this radiologic observation.

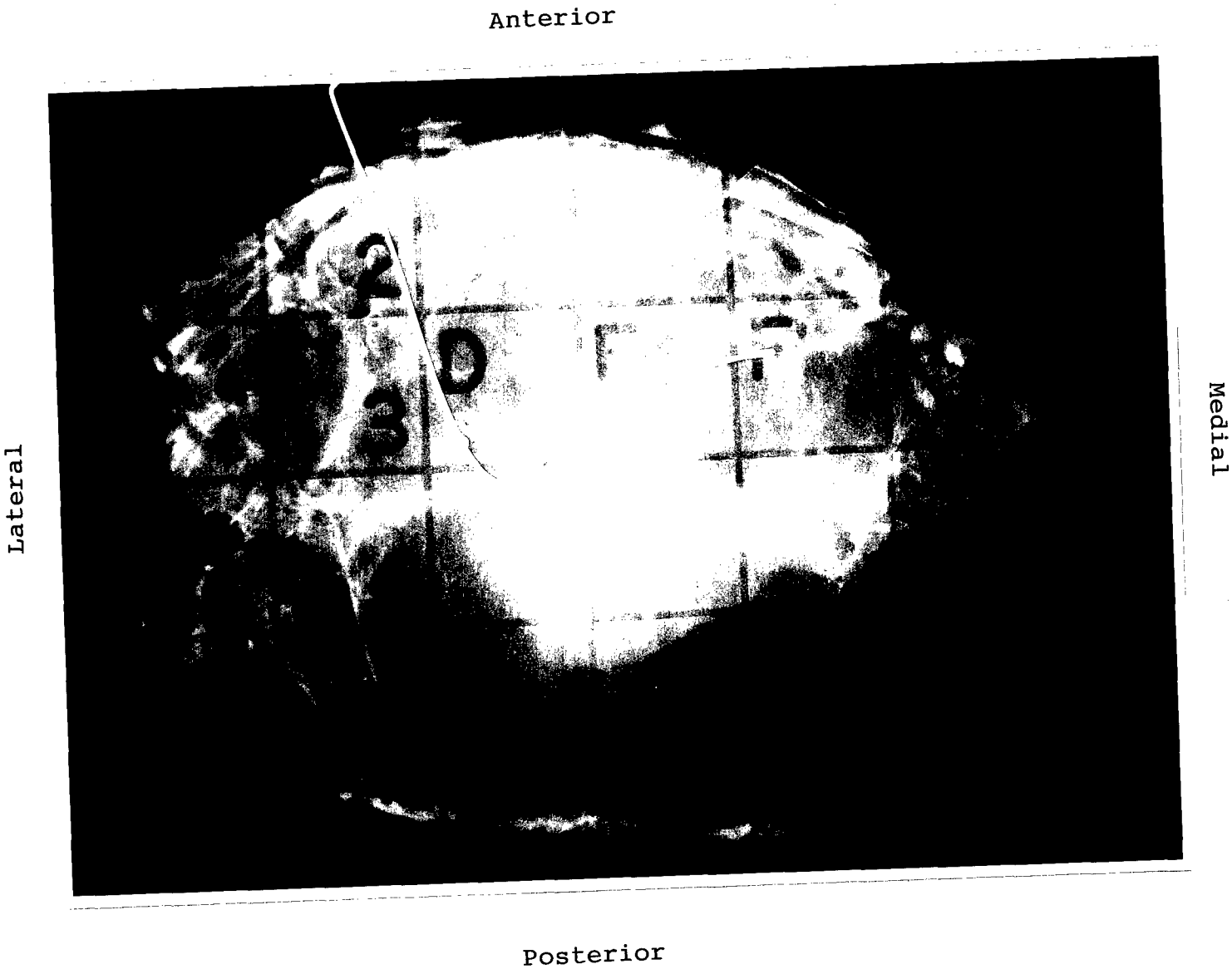
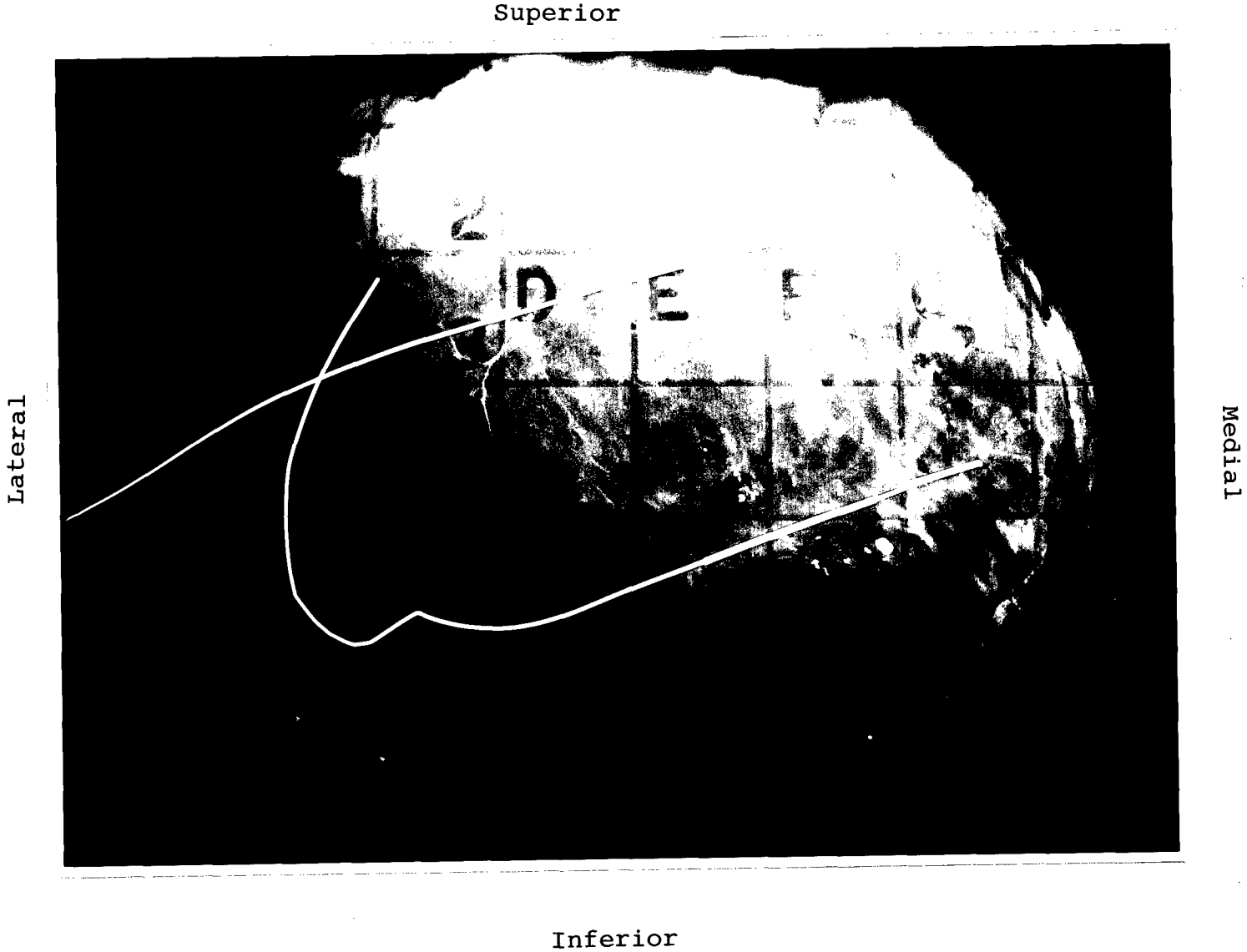


Figure 4. Widespread ductal carcinoma in-situ (DCIS) manifesting as diffuse microcalcifications within the specimen radiograph. Malignant-appearing calcifications are marked by the two hookwires. Note the punctate calcifications at the lateral and medial edges of the specimen (in the inferior half of the image). It is difficult to correlate which radiographically visible calcifications correspond to site(s) of DCIS.



DEPARTMENT OF THE ARMY
US ARMY MEDICAL RESEARCH AND MATERIEL COMMAND
504 SCOTT STREET
FORT DETRICK, MARYLAND 21702-5012

REPLY TO
ATTENTION OF:

MCMR-RMI-S (70-1y) 28 July 03

MEMORANDUM FOR Administrator, Defense Technical Information Center (DTIC-OCA), 8725 John J. Kingman Road, Fort Belvoir, VA 22060-6218

SUBJECT: Request Change in Distribution Statement

1. The U.S. Army Medical Research and Materiel Command has reexamined the need for the limitation assigned to technical reports written for this Command. Request the limited distribution statement for the enclosed accession numbers be changed to "Approved for public release; distribution unlimited." These reports should be released to the National Technical Information Service.

2. Point of contact for this request is Ms. Kristin Morrow at DSN 343-7327 or by e-mail at Kristin.Morrow@det.amedd.army.mil.

FOR THE COMMANDER:

Phyllis Rinehart

PHYLLIS M. RINEHART
Deputy Chief of Staff for
Information Management

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